USE OF AMBR250 AS A SMALL SCALE MODEL FOR MANUFACTURING-SCALE SINGLE-USE BIOREACTORS

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Quality by Design (QbD) has become an integral part of biopharmaceutical process development and manufacturing. To gain the enhanced process understanding required by QbD, a well-designed small scale model that accurately predicts behavior at manufacturing scale is essential. This process understanding should ideally be achieved with rapid, efficient experimentation to decrease both the time and cost required for development. The ambr250 automated microscale bioreactor system has the potential to address all of these challenges. By embedding the ambr250 into the upstream process development workflow, throughput can be dramatically increased allowing for greater exploration of parameter operating ranges and more complete process understanding. However, the value of such microscale technologies hinges on their ability to accurately mimic manufacturing scale.

We embarked on a study to demonstrate the applicability of the ambr250 (250 mL) as a small scale model for a 2000-L single-use bioreactor (SUB). We evaluated consistency of cell culture process performance from the ambr250 to 2000-L SUB scale along with intermediate scales such as our legacy small scale model (3-L glass stirred-tank reactors) and 50-L to 1000-L SUBs. Scalability was assessed using two monoclonal antibody molecules expressed from different CHO hosts (CHO K1 and DG44) and cultivated in different media platforms (chemically-defined and yeastolate-containing) to ensure broad applicability of the small scale model. Engineering principles were applied to develop appropriate agitation and gassing strategies at each scale to ensure comparability, with a power input based scaling strategy performing the best. Based on both univariate and multivariate data analysis methods the ambr250 behaved comparably to both our legacy small scale model and the SUBs for the assets evaluated. Areas of focus to further refine the ambr250 as a small scale model have also been identified.